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BY

W. B. CANNON AND S. W. BRITTON WITH THE COLLABORATION OF J. T. LEWIS AND A. GROENEVELD

*From the Laboratories of Physiology in the Harvard Medical School*

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# STUDIES ON THE CONDITIONS OF ACTIVITY IN ENDOCRINE GLANDS

## XX.[1] The Influence of Motion and Emotion on Medulliadrenal Secretion

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*From the Laboratories of Physiology in the Harvard Medical School*

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The great importance of emotional excitement in the determination of conduct, in the mobilizing of bodily forces, and in the disturbance of essential functions gives peculiar significance to a search for facts which might help to disclose its physiological nature. When the search is directed towards elucidating the rôle of an agent, such as adrenin is, which itself can extensively and deeply affect organic processes, it holds a special interest. There is, consequently, good reason for the vigor of the discussion which has continued throughout the past decade relative to the existence of an increased secretion from the adrenal medulla, particularly during intense emotional stress.

Review of literature. Fifteen years have passed since Cannon and de la Paz (1911) announced an emotional stimulation of medulliadrenal secretion. They noted that the beating intestinal strip was inhibited by blood taken from an excited animal, whereas it was not inhibited by blood taken from the same region of the same animal when calm. The next year (1912) Elliott reported that when he compared the adrenin content of the innervated with that of the denervated adrenal gland of cats excited by "$\beta$-tetra" or morphine, he found the content in the innervated gland much less than in the other. Furthermore, he observed that paradoxical dilatation of the pupil, which had been disconnected from the superior cervical ganglion, occurred even in slight anger when the adrenal relations were normal, but that no trace of the reaction remained in anger aroused after

[1] The paper entitled "A Lasting Preparation of the Denervated Heart," which was numbered XVII in this series, should have been numbered XIX; number XVII was published in This Journal, 1925, lxxiv, 291.

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1911

the glands had been excised. These results were regarded as bringing prompt support to the view that in fear and rage medulliadrenal secretion is increased.

Elliott's observations on the iris sensitized by removal of the superior cervical ganglion were confirmed by Kellaway (1919). The pupil on the operated side under bright illumination is usually smaller than its fellow. Kellaway laid special stress on the persistently *large* size of that pupil after a test and thereupon its much slower return to a small size, as compared with the normal. With splanchnic nerves intact and adrenal glands present the paradoxical dilatation occurred under excitement, but after the nerves were cut the reaction did not appear. Although the "paradox" was not marked, it was described as "definite."

In 1919 Cannon published electrical records of the effects of excitement on the rate of the heart, after vagus section and stellate removal, when the adrenals were active and again after they had been removed. A change from a calm state to excitement increased the rate 38 beats per minute under the former circumstances and only 4 beats after adrenalectomy. Hartman, McCordock and Loder (1923), using as an auto-indicator the completely denervated iris, reported very little if any increase in the output of adrenin in their cats when in the presence of a barking dog. They testified, however, that this was what might have been expected in animals which did not become excited, explained that there was indifference to the dog while the observers were near, and suggested that further tests should be made on cats unaccustomed to the laboratory.

Besides this more or less direct evidence regarding discharge of adrenin in strong emotional states there have been observations possessing inferential value. Cannon and Mendenhall (1914) reported that stimulation of the splanchnic nerves shortens the coagulation time of blood, just as injected adrenalin does, but that this effect fails if the adrenal glands have been removed; and, furthermore, they found that excitement induces faster clotting, but only so long as the splanchnic nerves are intact. It would appear, therefore, that excitement produced the phenomenon *via* increased medulliadrenal secretion. Also Lamson (1915) noted that fear or rage, as well as injection of adrenalin, evokes in cats polycythemia, but that emotional disturbance after removal of the adrenal glands causes no increase in the red-corpuscle count. Finally, Cannon and Britton (1925) described a method of destroying the lateral cerebral cortex and leaving the basal ganglia, thus producing a pseudaffective preparation which manifests in an acute experiment the physiological phenomena of great emotional excitement. In the pseudaffective state there is evidence of much augmented adrenal secretion, for with the adrenals intact the denervated heart beats very rapidly (averaging 252 beats per minute during activity), and after adrenal removal much more slowly (averaging 156

beats per minute). All these observations taken together are consonant with the view that in periods of tense excitement the adrenal medulla, like other viscera innervated by sympathetic fibers, is involved in the emotional response.

The foregoing review of the evidence favorable to emotional stimulation of an increased adrenin output shows that, besides being indicated by faster coagulation, polycythemia, and a more rapid pulse in the pseudaffective state, it is based on 1, the presence of changes in the adrenin content of the glands; 2, pupillary reactions, and 3, the effects of blood on the beating intestinal strip.

Opposed to this evidence are the experiments and conclusions of Stewart and Rogoff. In 1916 they confirmed Elliott's observations on the effects of morphine and "$\beta$-tetra" on the adrenin content in cats; but they drew different inferences. They first discounted the effects of morphine as being due to "fright," because they found that morphine lessens the adrenin content equally well in dogs which are not put into a state of "fright" by morphine, and also because they could not demonstrate any reduction of the adrenin store in cats excited for some time by barking dogs. Furthermore, they failed to confirm the paradoxical reaction,—in four cats observed by them the "denervated" iris and the normally innervated iris both enlarged, "instantaneously," in sudden fright after inactivation of the adrenals. Again (1917), they failed to confirm Cannon and de la Paz; they repeated in three animals the procedure employed, but the blood which they took from the excited animal, they stated, caused no inhibition of the rhythmically contracting intestine. In 1923, without further experimenting, they characterized the "exploits of the barking dog in frightening epinephrin out of the adrenals of a cat" as a "myth."

With regard to the action of the two drugs, morphine and "$\beta$-tetra," it may be admitted at once that they complicate the reaction. In cats and dogs they may directly stimulate adrenal secretion, and also they may prevent a restorative process which, in spite of discharge of adrenin, would maintain the supply (cf. Stewart and Rogoff, 1917). Evidence indicates that such a restorative process is normally operating. For example, Tscheboksaroff (1910) and Elliott (1912) observed that splanchnic stimulation, though it is known to produce abundant discharge, leaves a larger adrenin store in the stimulated than in the unstimulated gland. Further, Stewart and Rogoff (1916) reported that during prolonged, interrupted stimulation an amount of adrenin must have been formed in the gland equal to the initial load; and they also found (1919) that after the greatly increased output evoked by strychnine there is no difference in the residual adrenin content of the innervated and the denervated gland. As Stewart (1922) states, assays of the store of adrenin in the gland cannot be used directly as evidence regarding the discharge—"The store represents the

balance between epinephrin formed and epinephrin liberated, and a diminution in the store may be due either to diminished up-building or to increased discharge." From Stewart's own reasoning, therefore, the absence of any reduction of the store in the excited cats studied by him and Rogoff cannot be taken as proof that during the excitement no discharge occurred. The histological observations made on the adrenal medulla of frightened guinea pigs by Buscaino (1920) were negative and likewise not decisive. And the same comments may properly be made regarding the experiments reported by Uno (1922) who compared extracts of the adrenals taken from rats which had been fighting each other for some hours, with extracts taken from resting rats of the same litter. The results were negative. It should be clear that, confronted by positive evidence for adrenin secretion during emotional stress, all this testimony would have no pertinence whatever.

With regard to the pupillary reactions the difference between the observers is sharp. Elliott and Kellaway both state explicitly that the paradoxical pupillary response is present in excitement if the adrenal relations are normal, and that it disappears after adrenalectomy. Stewart and Rogoff saw no difference in the reaction of the "denervated eye" whether the adrenals were intact or inactivated. The main points which they make are that in the four cats with a "denervated eye" and with adrenal secretion eliminated dilatation of the pupil occurred "instantaneously," after an interval much too short for a humoral effect, and that it occurred in the "denervated eye" as well as in the normal eye. As Kellaway pointed out, it is not the rate of dilatation which is watched in the paradox, but the degree of dilatation and the speed of recovery. In the true response the pupil on the operated side becomes regularly larger than the normal and recovers more slowly. And as one of us (Cannon, 1915, p. 35) has remarked before, with regard to this testimony of Stewart and Rogoff, the eye still innervated by the third cranial nerve can hardly be regarded as "denervated;" the "instantaneous" dilatation of the "denervated" iris in rage, therefore, is readily explicable as due to central inhibition of the tonically active constrictor impulses. On the one hand, then, are the observations of Elliott and Kellaway, on excited animals before and after adrenalectomy, which led them to report the failure of the characteristic paradoxical pupillary response in the absence of medulliadrenal secretion; and on the other hand are the observations of Stewart and Rogoff that even after adrenal inactivation there occurs in excited animals a quick widening of the pupil—a phenomenon, however, properly accounted for by inhibition of constrictor tone. Doubtless this nervous factor was present as part of the paradoxical response, and to that extent the test is not above criticism. In the instantaneous change noted by Stewart and Rogoff, however, there is nothing which confutes the conclusions of Elliott and Kellaway that the paradoxical pupillary response signals increased adrenal secretion at times of emotional stress.

Stewart and Rogoff's failure in three attempts to obtain the results obtained by Cannon and de la Paz is not surprising. As already stated (Cannon, 1919), the method is difficult and exacting, and in the hands of the original investigators it was not successful until after considerable experience. The fact is manifest, however, that in their hands it did yield evidence of emotional stimulation of medulliadrenal secretion, and that in the hands of Stewart and Rogoff it did not. Even if Stewart and Rogoff had succeeded, the results, in their opinion, would not have been significant, for they (1920, p. 551) have argued that splanchnic vasoconstriction would cause "slowing of the blood flow in the inferior cava" and therefore greater concentration of the adrenin content without augmented secretion. This argument, it should be noted, is not accompanied by the slightest hint of evidence that the cava flow is in fact retarded. Indeed, Edwards' (1914) demonstration that splanchnic stimulation *increases* the blood flow in the external jugular and in the femoral veins, by 12.5 and 15 per cent respectively, thereby compensating for the check in the portal circuit, they dismiss with the remark that they are "not concerned" with it. Clearly, the faster flow in the inferior cava (associated with the faster flow in the femoral veins) would be unfavorable, rather than favorable, to the results obtained by Cannon and de la Paz. Stewart and Rogoff's further arguments, that those results might be due to the influence of respiration on the cava flow, or to massage of the adrenal medulla by the catheter in the cava, or to a happy placing of the eye of the catheter near an opening of the adrenal veins despite a carefully measured position above them, are so extremely hypothetical, so lacking in any factual support, that they need not be further considered.

The method. Because of the importance of bodily reactions in strong emotional states, and because of the difficulties which have been encountered in the use of the methods described above, it seemed worth while to attack the problem by way of another procedure. We have made use of the lasting preparation of the denervated heart, in animals operated upon by surgical methods and living normally, as described by Cannon, Lewis and Britton (1926). The results obtained by use of the denervated heart have been questioned by Stewart and Rogoff (1920). With reference to reflex stimulation or asphyxial stimulation, or both, these results, however, have recently been confirmed by Tournade and Chabrol (1925) in Algiers, working on a crossed circulation; by Houssay and Molinelli (1924, 1926) in Buenos Aires, also employing a crossed circulation; by Baschmakoff (1923) in Kazan, using the denervated salivary gland; by Hartman, McCordock and Loder (1923) in Buffalo, recording the changes in the completely denervated iris; by Anrep and Daly (1925) in London, studying the heart outside the body, but connected with the abdominal aorta and inferior vena cava; and by Kodama (1923), now supported by Sugawara,

Watanabé and Saito (1926), in Sendai, Japan, employing Stewart and Rogoff's own method. If support from anybody, anywhere, has been given to Stewart and Rogoff's observations and arguments, where? Their inference that the adrenin output continues at a uniform rate, unmodified by reflex stimulation and asphyxia, is wholly contradicted by experiments. On the other hand the concordant experience of investigators, derived from a variety of methods, justifies confidence in the response of the denervated heart as a sign of an increased discharge from the adrenal medulla.

The denervated heart is made to beat faster by increased adrenal, hepatic and thyroid secretion. When these sources of humoral stimulating factors are excluded the amount of acceleration in repeated extreme tests is slight (Cannon, Lewis and Britton, 1926). In order to observe the influence of any one of these humoral accelerators, therefore, it is only necessary to exclude the other two. Thyroid innervation through sympathetic connections is abolished by removal of the stellate ganglia (a part of the routine in denervating the heart). The discharge of the hepatic cardio-accelerating substance is excluded by severing the nerves on the duodeno-hepatic artery (Cannon and Uridil, 1921; Cannon and Griffith, 1922). Then medulliadrenal secretion alone remains to produce a faster heart rate. That this is true can readily be proved by removal of the right adrenal and denervation of the left, whereupon the acceleration ceases.

The lasting preparation of the denervated heart has important advantages over other methods. From it an almost continuous graphic record can be obtained, revealing the latent period of the response after any procedure, the moment of greatest activity, and its gradual subsidence. Instead of an observation on a single sample of blood, taken somewhat blindly, without knowledge of its relation to the total reaction, the total reaction can itself be followed; and not one experiment only, but as many as desired, in the same animal, all without the possibility of the profound depression which may attend anesthesia (cf. Cannon and Rapport, 1921, table 3; and Sugawara, Watanabé and Saito, 1926). And furthermore, after various tests have been repeated with the adrenal connections intact, the same tests on the same animal, after the adrenals have been inactivated, may be repeated as many times as before if that is desired, or until the proof is clear that the previous acceleration was due to a greater output of adrenin. The importance and the great advantage of making these observations on healthy vigorous animals, free from the influence of narcotics, and of controlling the observations on the same animals, cannot be emphasized too strongly.

The question arises as to the degree of reliance which may be placed on increases in the rate of the denervated heart in judging how widely the discharge of adrenin varies. That the preparation is a wholly satisfactory

zero instrument, showing whether the adrenin output is increased or not, has been proved in earlier experiments in this series (Cannon and Rapport, 1921; Cannon and Carrasco-Formiguera, 1922). But in those experiments the animals were quiet, under anesthesia. In active, vigorous animals can it reasonably be used to indicate differences in secretion? In answer to this question the following facts are pertinent. 1. Mere increase in the *amount* of adrenin-containing blood passing through the coronary vessels of the denervated heart in a given time, as caused by rise of blood pressure (see Markwalder and Starling, 1913), does not alter noteworthily the rate of beat. This was shown by Cannon and Rapport (1921, fig. 2) and confirmed by Anrep and Daly (1925). 2. Within limits the denervated heart responds to increasing *concentrations* of adrenin in the blood by an increasingly faster rate. Cannon and Rapport (1921) showed that repeated equal intravenous doses of adrenalin produce the same or nearly the same increments of heart rate (in an animal with the circulation confined to the trunk vessels) and that as the doses are made larger the cardiac accelerations become greater. A similar relation between adrenin concentration and the rate of beat was demonstrated by Anrep and Daly (1925) in the heart-lung preparation. 3. The circulation rate is normally faster during muscular activity than during rest (see Wiggers, 1923). In part this is due to a larger return of blood to the heart in a given time, and in part to a more rapid heart rate. The operation for denervating the heart leaves unchanged the factors which augment the return of blood from the periphery during muscular exertion. The isolated heart will put forth what it receives (cf. observations on the heart-lung preparation, Patterson and Starling, 1914). Therefore, during and immediately after activity there will be a faster circulation rate, even though the heart is not accelerated. According to Anrep and Daly (1925) variations in the circulation rate do not influence to an important degree the effect of adrenin on the rate of the isolated heart. Let us make two assumptions: *a*, that Stewart and Rogoff's conclusion is correct, i.e., that adrenin is secreted at a uniformly constant rate, not affected by afferent stimulation, asphyxia or emotional excitement; and *b*, that the secreted adrenin is destroyed as it passes through the systemic blood vessels (Elliott, 1905). Then, doubling the volume flow of blood would halve the concentration of adrenin. Anrep and Daly found that a change from 1 part of adrenin in 75 millions (approximately the ratio determined by Cannon and Rapport, 1921, in undisturbed experimental conditions) to 1 part in 150 millions lessened the increase of heart rate by only 6 beats per minute—the rate rose from 144 to 168 instead of from 144 to 174. Even when the concentration was reduced to one-fourth, which would result from quadrupling the volume flow, the effect was still not very great—144 to 162 instead of 144 to 174.

Although the faster circulation rate of muscular activity is not important

in reducing the influence of adrenin on the heart, it clearly does not favor a faster heart rate. It could do so only if the second of the two assumptions made above is wrong, i.e., only if the secreted adrenin is not destroyed. One might suppose that as the blood flows more rapidly the adrenin would pass, still potent, from the arteries to the veins, and that, thus accumulating and becoming more and more concentrated, it would cause a more rapid pulse. Invalidating that explanation is our repeated experience that the maximal effect appears promptly, within 20 or 30 seconds after a struggle, and thereupon the effect, instead of becoming larger, as would result from increasing accumulation, gradually becomes smaller. The facts, therefore, are opposed to the view that concentration of adrenin rises because it is not destroyed.

Since adrenin does not accumulate in the blood by escaping destruction, the faster heart rate after struggle leaves no other inference than that it is due to increased concentration resulting from increased discharge. Thus the first of the two assumptions made above, i.e., the correctness of Stewart and Rogoff's claim that the discharge is constant and unvarying, is shown to be unwarranted.

On the basis of the foregoing considerations it is possible to go still further. The minute-volume flow of blood rises gradually as exertion becomes gradually more intense (Douglas and Haldane, 1922). Thus the cardiac acceleration would become gradually slower if the adrenin output were constant. In fact, however, as activity becomes more vigorous the denervated heart beats gradually faster. The faster beat, then, occurs in spite of a faster circulation rate, and becomes still more rapid as the circulation rate rises still higher. In other words, as other conditions become less and less favorable to a quickening of the heart beat by an increased secretion of adrenin, the evidence for increased secretion becomes more and more pronounced. We see no other conclusion to draw from these observations than that as an animal manifests greater activity the adrenin output is greater. These points will be illustrated as the results of our experiments are examined.

Results. Three types of activity have been studied by us as associated with increased secretion from the adrenal medulla—minor movements with little or no affective accompaniment; emotion, with little or no movement of skeletal muscles; and a combination of the two in vigorous activity with excitement. The rate of the denervated heart was augmented in each of these states, but to different degrees.

In order to have some indication of the relative amount of cardiac acceleration under various circumstances it was necessary to establish a basal or standard rate. This was done by bringing the animal to a calm, quiet state while resting on a cushion held in the lap. The cat usually lay comfortably on one side, and without protest permitted the receiving

tambour to be held against the chest wall where the cardiac impulse was most prominent. The heart rate first recorded, after the animal with active adrenals was placed on the cushion, was regularly faster than it was later, for reasons which presently will be understood. Usually within five or ten minutes, if the animal remained quiet, the rate fell (the average fall was 16 beats) until it reached a constant low level. This was the basal rate. The changes of rate due to the various types of action mentioned above were referred back to the basal for comparison.

*The effect of minor movements, without notable emotion.* The observations of Hartman, Waite and Powell (1922) had furnished evidence that adrenal secretion is increased during muscular exercise. We were surprised to note, however, that even slight motions, such as extending the legs ("stretching"), or turning the body, or lifting the head, were attended by increase of heart rate. We thereupon induced such minor activities by lowering the cushion to the floor and letting the cat walk for a minute or two. The animal was then picked up gently, replaced on the cushion, and the heart rate recorded as soon as possible. In table 1 and in figures 1 and 2 are displayed results of these experiments.

Examination of table 1 shows that, with the exception of two instances in which the heart rate increased 18 and 24 beats, slight spontaneous activity, while the animal with intact adrenals was resting on the cushion, was followed by an increase of rate between 5 and 10 beats per minute. This result might be regarded as accidental, if it had not occurred regularly under the circumstances mentioned, and if it had not failed to occur after the adrenals were inactivated (see table 1).

When the animals were allowed to walk, the acceleration was greater. In one instance the heart beat was faster by 38 beats after a walk of two minutes, and in four other of the 14 observations the rise was above 20. These increases were unusual, however, and may have resulted from disturbance when the animals were picked up again in order to record their cardiac pulsations. As a rule the walking raised the rate between 10 and 20 beats. Cat 38 consistently showed large increases, and on four occasions the rise averaged 27 beats per minute. After inactivation of the adrenals the acceleration either failed to occur or was small (see table 1 and fig. 1).

The average cardiac acceleration in 27 observations on the effect of minor movements, without notable emotion, was 15 beats per minute. The variations ranged between 6 and 38 beats. After the adrenals were inactivated the average acceleration in 23 tests under the same conditions was 1, with variations between −2 and 5 (see fig. 2).

*The effect of emotional excitement, with slight muscular activity.* This condition was induced in two ways: by bringing an aggressive dog near the cat while it was resting quietly on the cushion, and by fastening the cat

TABLE 1

*Changes of rate of the denervated heart accompanying minor movements, without notable emotion*

| ADRENALS ACTIVE | | | | | ADRENALS INACTIVE | | | | |
|---|---|---|---|---|---|---|---|---|---|
| Cat number, date | Basal heart rate, quiet on lap | Increase after slight activity on lap | Increase after brief walk | Remarks | Cat number, date | Basal heart rate, quiet on lap | Increase after slight activity on lap | Increase after brief walk | Remarks |
| (23) | | | | | (23) | | | | |
| Jan. 21 | | | | Heart denervated | Feb. 11 | | | | Adrenals inactivated |
| Jan. 26 | 120 | 18 | | | Feb. 17 | 88 | 0 | | |
| Jan. 27 | 116 | 8 | | Slight restlessness | Mar. 4 | 104 | 0 | | |
| Feb. 3 | 112 | 8 | | | | | | | |
| (26) | | | | | (26) | | | | |
| Mar. 2 | | | | Heart denervated | Mar. 25 | | | | Adrenals inactivated |
| Mar. 19 | 116 | | 10 | Walked 10 steps | Mar. 26 | 120 | | 4 | |
| Mar. 20 | 92 | 24 | | Played ½ minute | Mar. 30 | 108 | 0 | 0 | Walked 1 minute |
| Mar. 20 | | | 24 | Walked ½ minute | Apr. 1 | 104 | 0 | | |
| Mar. 22 | 90 | 8 | | Slightly restless | | | | | |
| (27) | | | | | (27) | | | | |
| Mar. 3 | | | | Heart denervated | Apr. 6 | | | | Adrenals inactivated |
| Mar. 13 | 144 | 6 | | Restless | Apr. 7 | 94 | | 0 | Walked 2 minutes |
| Mar. 18 | 120 | | 20 | Walked 5 steps | Apr. 10 | 108 | | 0 | Walked 4 minutes |
| Apr. 6 | 96 | | 38 | Walked 2 minutes | Apr. 13 | 92 | 0 | | |
| | | | | | Apr. 16 | 118 | | 2 | |
| (33) | | | | | (33) | | | | |
| Mar. 23 | | | | Heart denervated | Apr. 30 | | | | Adrenals inactivated |
| Apr. 12 | 122 | | 10 | Walked 1 minute | May 1 | 128 | −2 | | Slight activity |
| Apr. 16 | 118 | 6 | | Restless | May 2 | 128 | 0 | | |
| Apr. 16 | | | 16 | Walked 2 minutes | | | | | |

| | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|
| (38) | | | | | (38) | | | | |
| May 12 | | | | Heart denervated | June 4 | | | | Adrenals inactivated |
| May 27 | 150 | 6 | | Stretching, pawing | June 5 | 120 | 2 | 4 | |
| May 27 | | | 18 | | June 7 | 144 | −2 | | Stood up, stretched limbs |
| June 1 | 118 | 10 | 26 | | June 7 | | | 2 | |
| June 2 | 128 | | 34 | Walked ½ minute | | | | | |
| June 4 | 130 | | 30 | | | | | | |
| (46) | | | | | (46) | | | | |
| June 11 | | | | Heart denervated | June 24 | | | | Adrenals inactivated |
| June 19 | 128 | 10 | 16 | | June 25 | 112 | 0 | | Turned over |
| June 21 | 124 | 6 | | Stretched limbs few times | June 25 | | | 5 | |
| June 21 | | | 14 | | June 28 | 100 | 2 | | |
| (49) | | | | | (49) | | | | |
| June 10 | | | | Heart denervated | June 24 | | | | Adrenals inactivated |
| June 19 | 118 | 10 | 14 | | June 25 | 114 | 0 | | Stood up, prepared to jump from lap |
| June 21 | 100 | 6 | | Playful | | | | | |
| June 21 | | | 10 | | June 25 | | | 4 | |
| | | | | | June 28 | 101 | 1 | | Walked 1 minute |
| | | | | | June 28 | | | 3 | |

back downward in a comfortable holder. Usually when the dog approached the resting cat and began to bark, the cat showed some or all of the following signs of excitement—dilatation of the pupils, erection of hairs on the tail and back, retraction of the ears, baring of the teeth,

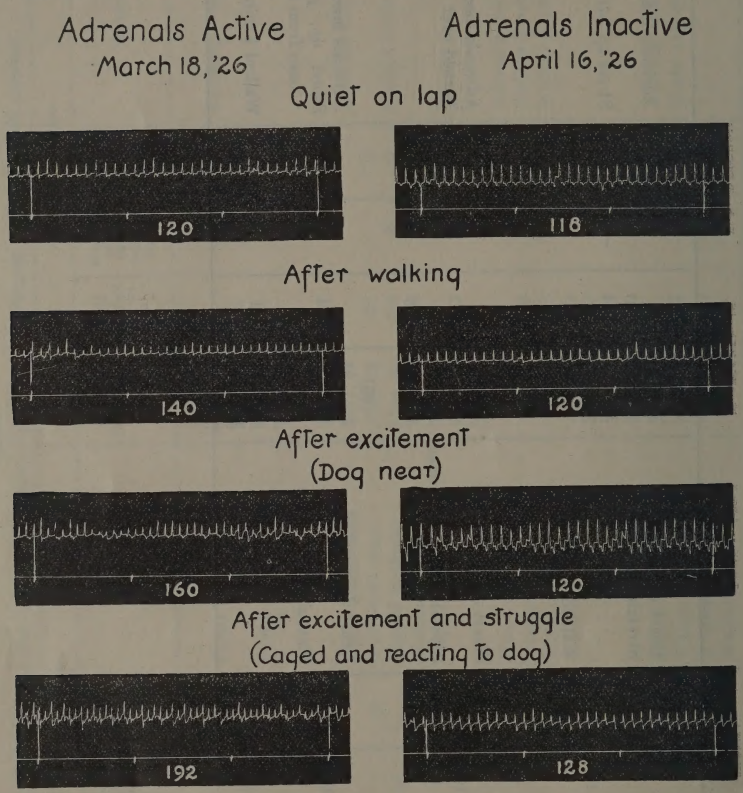


Fig. 1. Original records of the rate of the denervated heart of cat 27 taken before (on March 18) and after (on April 16) medulliadrenal secretion was excluded (on April 6). Time in 5-second intervals. The basal rate with the animal quiet on lap is to be compared with the rate after walking, after being excited by the presence of a dog, and after caged and reacting to a barking dog.

hissing, snarling, spitting, and striking at the dog with one paw or sometimes with both paws in rapid succession, with claws protruding. When the animal was placed in the holder, motion of the neck was limited by two

upright rods which were closed above by a cross-bar; the fore legs were restrained loosely in thongs which passed through holes in the side of the holder; the hind legs were not fastened, but were grasped between the

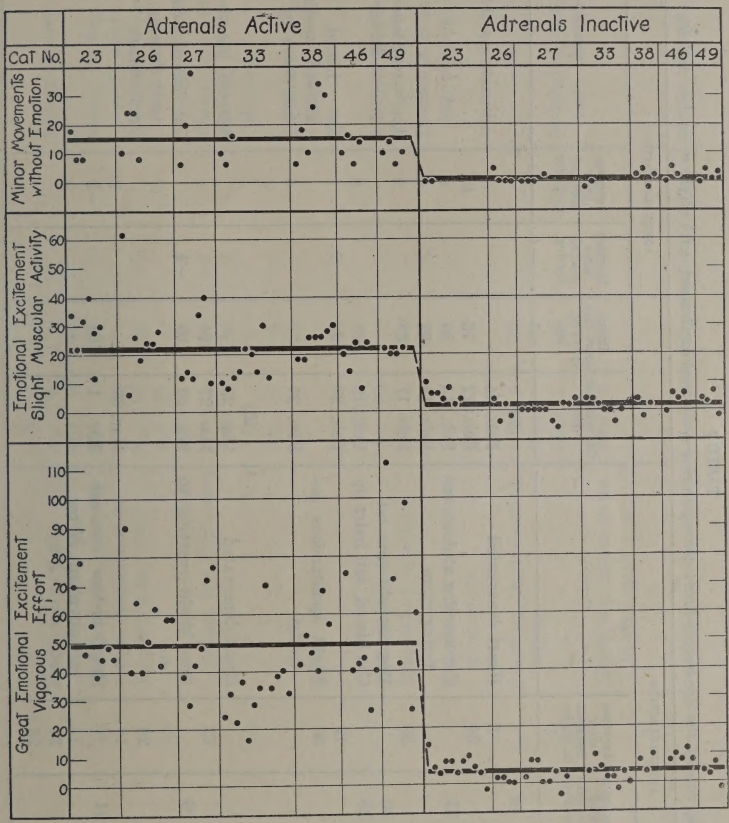


Fig. 2. Graphic record of the results presented in tables 1, 2 and 3. The dots represent increases of rate of the denervated heart above the basal level that followed *a*, minor movements without notable emotion; *b*, emotional excitement with slight muscular activity, and *c*, great emotional excitement with vigorous effort, before and after inactivation of the adrenal medulla. The wide line indicates in each condition the average of the changes of heart rate.

fingers of one of the observers. The usual behavior of the animal under these circumstances was characterized by minor indications of disturbance—uneasy twitching of the tail, occasional mewing, and turning of the

TABLE 2

*Changes of rate of the denervated heart accompanying emotional excitement, with slight muscular activity*

| ADRENALS ACTIVE | | | | | ADRENALS INACTIVE | | | | |
|---|---|---|---|---|---|---|---|---|---|
| Cat number, date | Basal heart rate, quiet on lap | Increase after excited by dog | Increase after fastened to holder | Remarks | Cat number, date | Basal heart rate, quiet on lap | Increase after excited by dog | Increase after fastened to holder | Remarks |
| (23) | | | | | (23) | | | | |
| Jan. 21 | | | | Heart denervated | Feb. 11 | | | | Adrenals inactivated |
| Jan. 27 | 116 | | 34 | | Feb. 12 | 76 | | 10 | |
| Jan. 29 | 104 | 22 | | Cat saw dog at door, entering room | Feb. 13 | 80 | | 6 | |
| | | | | | Feb. 15 | 78 | | 6 | |
| Jan. 29 | | | 32 | | Feb. 17 | 88 | | 4 | Active resistance on being tied to holder |
| Jan. 29 | 104 | 40 | | Dog brought near cat | | | | | |
| Feb. 3 | 112 | 28 | | Cat hissed, tail hairs up | Feb. 19 | 86 | | 8 | |
| Feb. 3 | | | 12 | | Feb. 23 | 108 | 2 | | Cat hissed, growled, showed teeth, lashed tail, hairs up |
| Feb. 5 | 90 | | 30 | Slight spontaneous activity | Feb. 23 | | | 4 | |
| (26) | | | | | (26) | | | | |
| Mar. 2 | | | | Heart denervated | Mar. 25 | | | | Adrenals inactivated |
| Mar. 8 | 146 | | 62 | | Mar. 27 | 104 | | 4 | |
| Mar. 10 | 128 | 6 | | Very slight reaction to dog | Mar. 30 | 108 | −4 | | Cat hissed, ears back, teeth showing, no major movements |
| Mar. 10 | | | 26 | | | | | | |
| Mar. 16 | 120 | | 18 | | Mar. 30 | | | 2 | |
| Mar. 18 | 98 | 24 | | Dog 6 meters from cat, no movement of cat | Apr. 1 | 104 | | −2 | |
| Mar. 19 | 116 | | 24 | | | | | | |
| Mar. 25 | 104 | | 28 | | | | | | |

| | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|
| (27) | | | | | (27) | | | | |
| Mar. 3 | | | | Heart denervated | Apr. 6 | | | | Adrenals inactivated |
| Mar. 8 | 144 | | 12 | | Apr. 7 | 96 | | 0 | |
| Mar. 10 | 148 | | 14 | Poor reaction; recovery from operation slow | Apr. 8 | 104 | 0 | 0 | Struck at dog 3 times, showed teeth |
| Mar. 13 | 140 | | 12 | Very quiet on holder | Apr. 10 | 100 | 0 | | Hissed and struck at dog |
| Mar. 16 | 130 | | 34 | | Apr. 10 | | | 0 | |
| Mar. 18 | 120 | 40 | | Cat jumped on floor, walked few steps, then retaken | Apr. 12 | 112 | −4 | | Hairs erect, hissing |
| | | | | | Apr. 13 | 103 | −6 | | Marked reaction |
| | | | | | Apr. 16 | 118 | 2 | | Hissing, striking, teeth showing |
| Apr. 6 | 92 | | 10 | | | | | | |
| | | | | | Apr. 17 | 116 | | 2 | |
| | | | | | Apr. 20 | 124 | | 4 | Vigorous struggle on holder |
| (33) | | | | | (33) | | | | |
| Mar. 23 | | | | Heart denervated | Apr. 30 | | | | Adrenals inactivated |
| Apr. 10 | 116 | | 10 | Respiratory infection, cat inactive | May 1 | 124 | | 4 | |
| | | | | | May 2 | 128 | 4 | | Excited 2 minutes, hissing, striking, hairs up |
| Apr. 12 | 122 | 8 | | Crouching, no general movements | | | | | |
| Apr. 12 | | | 12 | | May 2 | | | 2 | |
| Apr. 16 | 118 | 14 | | Hairs up, teeth showing, hissing | May 3 | 124 | | 0 | |
| | | | | | May 5 | 122 | | 0 | |
| Apr. 16 | | | 22 | | May 7 | 122 | | −4 | Struggling about 15 seconds |
| Apr. 26 | 132 | | 20 | | | | | | |
| Apr. 28 | 120 | 14 | | Crouching, hissed twice, showed teeth | May 8 | 130 | | 0 | |
| Apr. 28 | | | 30 | | | | | | |
| Apr. 30 | 124 | | 12 | | | | | | |

TABLE 2—*Concluded*

| ADRENALS ACTIVE | | | | | ADRENALS INACTIVE | | | | |
|---|---|---|---|---|---|---|---|---|---|
| Cat number, date | Basal heart rate, quiet on lap | Increase after excited by dog | Increase after fastened to holder | Remarks | Cat number, date | Basal heart rate, quiet on lap | Increase after excited by dog | Increase after fastened to holder | Remarks |
| (38) | | | | | (38) | | | | |
| May 12 | | | | Heart denervated | June 4 | | | | Adrenals inactivated |
| May 24 | 144 | | 18 | | June 5 | 120 | | 4 | |
| May 27 | 150 | 18 | | Cat very excited | June 7 | 144 | | −2 | Crying and jerking on holder |
| May 27 | | | 26 | | | | | | |
| May 28 | 130 | | 26 | | June 9 | 138 | | 2 | |
| June 2 | 128 | 26 | | Withdrew from dog, but hairs erect | | | | | |
| June 2 | | | 28 | | | | | | |
| June 4 | 130 | | 30 | | | | | | |
| (46) | | | | | (46) | | | | |
| June 11 | | | | Heart denervated | June 24 | | | | Adrenals inactivated |
| June 19 | 128 | | 20 | | June 25 | 112 | | 6 | |
| June 21 | 124 | 14 | | Hairs erect, no aggression shown | June 28 | 100 | 0 | 4 | |
| | | | | | July 2 | 106 | | 6 | Vigorous resistance on holder |
| June 21 | | | 24 | | | | | | |
| June 24 | 126 | 8 | | Moderate reaction to dog | | | | | |
| June 24 | | | 24 | | | | | | |
| (49) | | | | | (49) | | | | |
| June 10 | | | | Heart denervated | June 24 | | | | Adrenals inactivated |
| June 19 | 118 | | 22 | | June 25 | 114 | | 4 | Very vigorous struggle |
| June 21 | 100 | 20 | | Hissing, striking, etc. | June 28 | 101 | 3 | | Good response when dog near |
| June 24 | 118 | 20 | | Dog afraid of cat, but cat showed defensive attitude | June 28 | | | 7 | |
| | | | | | June 30 | 110 | | −2 | |
| June 24 | | | 22 | | | | | | |

head from one side to the other. At times the animal immediately resisted the strange position and the restraint, and struggled vigorously. This violent reaction we are not concerned with now; we are interested in what accompanies the little signs of excitement just mentioned, such signs as may be associated with complete cessation of gastro-intestinal movements (Cannon, 1911). In whatever manner the cat was excited the heart rate was recorded as soon as possible thereafter; within a minute after the dog had been taken away, and almost immediately after the cat was attached to the holder.

Reference to table 2 and to figures 1 and 2 shows the effects on the heart rate when emotional reactions occurred which were not attended by considerable contractions of skeletal muscles. Although the rise of rate may be slight when the cat is barked at by the dog, it is usually greater than when there is motion without excitement,—ranging between approximately 15 and 30 beats per minute instead of the 10-to-20-beat acceleration recorded after walking. It is noteworthy that when the cardiac response was small there was only a minor reaction to the presence of the dog (e.g., no. 26, March 10), and when the response was large the reaction was much more marked, with evidence of sympathetic activity in the standing hairs and the dilated pupils (e.g., no. 23, February 3).

The heart was made to contract somewhat faster by attaching the animal back-downward to the holder. In these circumstances the outward signs of disturbance varied considerably. Some animals took the experience relatively calmly from the beginning (cf. no. 27, March 8, 10, 13). Others were excited at first, and as they gradually became accustomed to the unnatural position were less perturbed by it (cf. no. 23, January 27, 29 and February 3; also no. 26, March 8, 10, 16). Corresponding with these variations of emotional reaction were the degrees of cardiac acceleration. The figures 10 to 35 cover most of the increments of heart rate that were observed, though in cat 26 the first confinement in the holder called forth a rise of 62 beats per minute.

The above increments in heart rate occurred when the adrenal medulla was undisturbed; in striking contrast were the cardiac responses after medulliadrenal inactivation. The animals were repeatedly subjected to the same conditions as before. The obvious reactions were precisely those which had previously been seen—hissing, growling, baring of the teeth and erection of the hairs when the dog approached the cat or barked and made aggressive motions; and twitching of the tail, mewing, and signs of uneasiness when the cat was fastened in the holder. Yet, as shown by the results in table 2 and as illustrated in figure 1, the heart rate, instead of rising sharply 30 or 35 beats per minute, decreased somewhat (see no. 27, April 12, 13), or remained unchanged (see no. 33, May 3, 5, 8), or showed a minor acceleration (see no. 23, February 12–23).

The average increment of cardiac pulsation in the 45 observations on the effect of emotional excitement, with only slight muscular activity, was 22 beats per minute. After the right adrenal gland had been removed and the left denervated the average increment in 39 observations was 1.8 if the decreases of rate are subtracted from the increases, and 2.5 if the decreases are given no value (see fig. 2 in which the average is marked at 2).

In connection with the effects of excitement, accompanied by little or no activity of skeletal muscle, some incidental observations on cardiac reactions of the cat in the presence of mice and rats are pertinent. Cat 26 had a basal rate of 92 at 9:55, March 20. A "catnip mouse" was brought near. The cat stood up on the cushion and played with the "mouse" for about 30 seconds. It was then removed. At 10:00 the heart rate was 116; at 10:04, 112; and at 10:06, 108. Again at 10:25, when the basal rate was 96 as the cat was lying on the cushion, a small cage containing a white mouse was brought near. The cat turned his head to one side, kept his eyes on the mouse as it moved about, and, though not rising or moving on the cushion, reached towards the mouse with a fore paw. This lasted from 10:27 to 10:29 when the cage was taken away. At 10:29 the heart rate had risen 20 beats (to 116); at 10:31, it was 116; at 10:34, 100; and at 10:36, 96.

Similar responses were observed in cat 27. On April 6, at 12:15, while the cat was quiet on the cushion the heart rate was 96. At 12:15½ a small cage containing a white rat was brought near. The cat showed some signs of interest, but did not make gross movements. At 12:17 the heart rate was 112. The rat was then taken from the cage and held near the cat. He lunged towards it, and not reaching it, sniffed (12:19). The rat was removed. At 12:20 the heart rate was 116; at 12:22, 108; at 12:24, 98. The catnip mouse was then dangled above the cat, which caught it and bit it. At 12:29, the heart rate was 114; at 12:30, 112; and at 12:33, 104. As shown by the control observations detailed in table 2 and figure 1, the denervated heart, after adrenal inactivation, would accelerate only 1 or 2 beats per minute, instead of 20 or more beats as above, in response to such minor excitement.

*The effect of great emotional excitement, with vigorous muscular effort.* Two methods were employed to bring about energetic movements combined with extreme emotional excitement. The cat was shut in a wire cage where it was barked at and attacked by a dog outside; or it was fastened into the holder, as described above, where it struggled either spontaneously or because of brief pressure near the root of the tongue. The experience in the cage seldom continued more than a minute. Of course the cat could not be injured inside its wire protection. As the dog rushed about the enclosure, however, the cat shifted its position quickly, keeping the enemy in view, now crouching, now counter-attacking, hissing, spitting, growling,

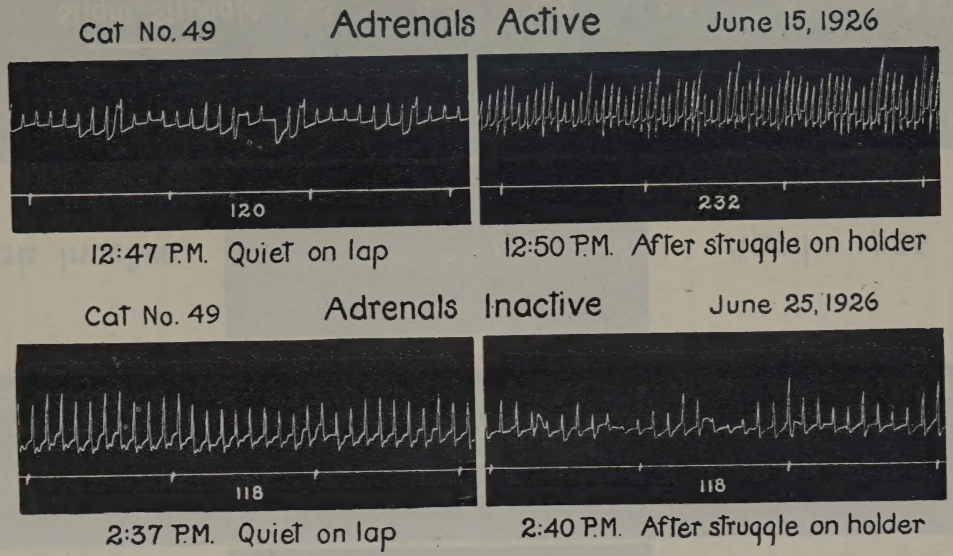


Fig. 3. Original records of cat 49 to show a maximal increase of rate of the denervated heart (112 beats per minute) that resulted from vigorous struggle, June 15, when the adrenals were active and the animal was fastened to the holder, and the absence of any increase, when, on June 25, with adrenals inactive, a correspondingly vigorous struggle was induced in the same manner. The interval between the records in each condition was 3 minutes. Time marked in 5 seconds.

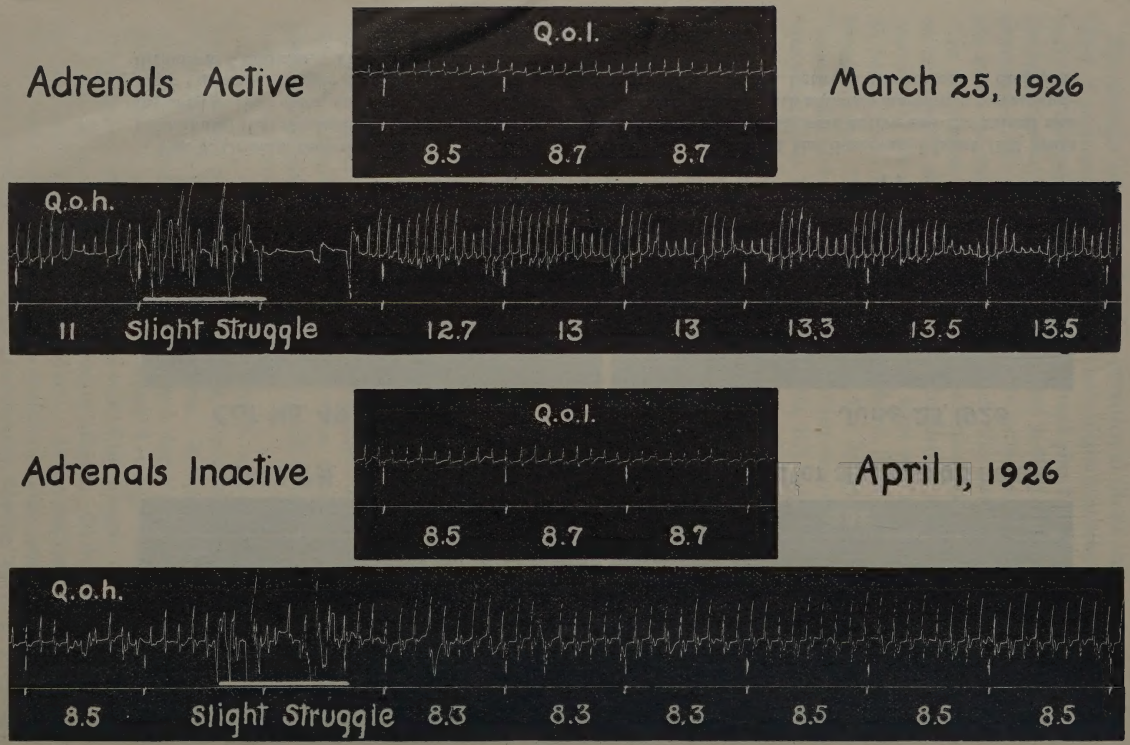
Adrenals Active
Q.o.l.
March 25, 1926
8.5 8.7 8.7
Q.o.h.
11 Slight Struggle 12.7 13 13 13.3 13.5 13.5
Adrenals Inactive
Q.o.l.
April 1, 1926
8.5 8.7 8.7
Q.o.h.
8.5 Slight Struggle 8.3 8.3 8.3 8.5 8.5 8.5

Fig. 4

striking, with ears drawn down, teeth showing, back arched, pupils widely dilated, hairs on the back erect and tail enormous. Immediately after the "fight" ended, the cat was removed from the cage, placed on the cushion and the heart rate recorded. The struggle in the holder has already been described (Cannon, Lewis and Britton, 1926). It was usually violent while it lasted—characterized by jerking the fore legs in the thongs, pulling and pushing the hind legs in the assistant's fingers, snarling, biting at the cross-bar and exhibiting every sign of resentful rage—but it rarely lasted more than 5 or 10 seconds and was usually followed by a period of quiet during which a good record of the heart rate could at once be obtained.

The results recorded in table 3 and illustrated in figures 1, 2, 3 and 4 reveal immediately how greatly the heart is accelerated when, with adrenals intact, vigorous action or struggle is combined with excitement. If the early observations on no. 33 (while it had a respiratory infection) are excluded, the minimal increase of rate was 26 beats per minute, the maximal 72, after the cat had been caged and barked at by the dog. It was not possible to obtain an immediate record of the pulse, and probably the maximal was higher than that set down in the table. In round numbers the increment of rate may be considered conservatively as ranging usually between 30 and 50 beats per minute—the average increase in 18 observations was 38.

A still greater response than this is usually seen when the cat struggles in the holder (see figs. 3 and 4). Again with no. 33 excluded, the increases of heart rate varied between 38 and 112, with eleven observations between 60 and 100. A rough statement of the extent of variation of the increment due to a mad and violent effort would be 40 to 80 beats per minute—26 of the 35 observations lie within that range. After adrenal inactivation the maximal rise of rate was 14 beats in two tests; in all the other 40 tests 8 beats or fewer were usually recorded, and in a few instances the heart actually worked more slowly after the struggle (see fig. 4).

The average speeding up of the denervated heart in 53 observations on the effect of great emotional excitement attended by vigorous muscular effort was 49 beats per minute. In 43 observations after adrenal inactivation the average was 4.5 if the decreases of rate are subtracted from the

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Fig. 4. Original records of cat 26, to show the short latent period and the gradual development of the maximal response. On March 25 with the adrenals active the basal rate (quiet on lap—*q. o. l.*) was 104 beats per minute, and when quiet on the holder (*q. o. h.*) the rate was 132; after a slight struggle (shown by irregularities in the record) it rose to 152.5 within fifteen seconds, and at the end of thirty seconds after the start of struggle it was 162—an increase of 58 beats per minute. The adrenals were inactivated on March 25, after the foregoing records were made. On April 1, with the same basal rate (104), the rate *q. o. h.* was 102, and a similar slight struggle was followed by a drop to 99.5 and then a gradual rise to 102.

TABLE 3

*Changes of rate of the denervated heart accompanying great emotional excitement, with vigorous muscular effort*

| ADRENALS ACTIVE | | | | | ADRENALS INACTIVE | | | | |
|---|---|---|---|---|---|---|---|---|---|
| Cat number, date | Basal heart rate, quiet on lap | Increase after caged and excited by dog | Increase after struggle on holder | Remarks | Cat number, date | Basal heart rate, quiet on lap | Increase after caged and excited by dog | Increase after struggle on holder | Remarks |
| (23) | | | | | (23) | | | | |
| Jan. 21 | | | | Heart denervated | Feb. 11 | | | | Adrenals inactivated |
| Jan. 26 | 120 | | 70 | Struggle while held on lap only | Feb. 12 | 76 | | 14 | Condition good |
| | | | | | Feb. 13 | 80 | | 6 | |
| Jan. 27 | 116 | | 78 | | Feb. 15 | 80 | | 4 | 20 seconds' vigorous struggle |
| Jan. 29 | 104 | 46 | | Back and tail hairs rough, good reaction | | | | | |
| Jan. 29 | | | 56 | | Feb. 17 | 88 | | 8 | |
| Feb. 3 | 112 | 38 | | Hissing, snarling, tail very big | Feb. 19 | 86 | | 8 | |
| | | | | | Feb. 23 | 108 | 4 | | Cat struck at dog, tail enormous |
| Feb. 3 | | | 44 | | | | | | |
| Feb. 5 | 90 | | 48 | | Feb. 23 | | | 8 | |
| Feb. 9 | 92 | | 46 | | Feb. 25 | 78 | | 10 | |
| | | | | | Mar. 1 | 114 | | 6 | Struggling 15 seconds |
| | | | | | Mar. 4 | 104 | | 4 | |
| | | | | | Mar. 8 | 114 | | −2 | |

| | | | | | | | | |
|---|---|---|---|---|---|---|---|---|
| (26) | | | | | (26) | | | |
| Mar. 2 | | | | Heart denervated | Mar. 25 | | | Adrenals inactivated |
| Mar. 8 | 146 | | 90 | | Mar. 27 | 104 | 2 | |
| Mar. 10 | 128 | 40 | | Hissing, tail and back hairs up | Mar. 30 | 108 | 2 | Ears back, teeth showing, hissing, spitting, striking |
| Mar. 10 | | | 64 | | | | | |
| Mar. 13 | 120 | | 40 | | Mar. 30 | | 0 | |
| Mar. 15 | 120 | | 50 | Vigorous spontaneous struggle | Apr. 1 | 104 | −2 | No increase in rate after several struggles |
| Mar. 18 | 98 | 62 | | Striking at dog, hissing, hairs up | | | | |
| Mar. 19 | 116 | 42 | | Usual reaction to dog | | | | |
| Mar. 19 | | | 58 | | | | | |
| Mar. 25 | 104 | | 58 | | | | | |
| (27) | | | | | (27) | | | |
| Mar. 3 | | | | Heart denervated | Apr. 6 | | | Adrenals inactivated |
| Mar. 8 | 144 | | 38 | | Apr. 7 | 94 | 2 | |
| Mar. 10 | 148 | 28 | | Hissing, growling, spitting, striking, tail and back hairs up | Apr. 8 | 104 | 8 | Very reactive, hissing, striking, hairs up |
| | | | | | Apr. 8 | | 8 | |
| Mar. 13 | 140 | | 42 | | Apr. 10 | 100 | 0 | Cat very aggressive, marked reactions |
| Mar. 16 | 130 | | 48 | | | | | |
| Mar. 18 | 120 | 72 | | Vigorous reaction | Apr. 10 | | 0 | |
| Apr. 6 | 96 | | 76 | | Apr. 16 | 118 | 10 | |
| | | | | | Apr. 17 | 114 | 4 | |
| | | | | | Apr. 20 | 124 | −4 | Vigorous struggle 20 seconds |
| | | | | | Apr. 28 | 112 | 2 | |

TABLE 3—*Concluded*

| ADRENALS ACTIVE | | | | | ADRENALS INACTIVE | | | | |
|---|---|---|---|---|---|---|---|---|---|
| Cat number, date | Basal heart rate, quiet on lap | Increase after caged and excited by dog | Increase after struggle on holder | Remarks | Cat number, date | Basal heart rate, quiet on lap | Increase after caged and excited by dog | Increase after struggle on holder | Remarks |
| (33) | | | | | (33) | | | | |
| Mar. 23 | | | | Heart denervated | Apr. 30 | | | | Adrenals inactivated |
| Apr. 1 | 120 | 24 | 32 | Cat has rhinitis, apathetic | May 1 | 124 | | 4 | |
| | | | | | May 2 | 128 | 10 | | Cat very excited, usual display |
| Apr. 10 | 116 | 22 | 36 | Health improved | | | | | |
| Apr. 12 | 122 | 16 | 28 | Moderate excitement only | May 2 | | | 6 | |
| Apr. 16 | 118 | 34 | 70 | | May 3 | 124 | | 2 | |
| Apr. 26 | 132 | | 34 | | May 5 | 122 | | −2 | |
| Apr. 28 | 120 | 38 | 40 | Usual reaction | May 7 | 122 | | 4 | Vigorous struggle |
| Apr. 30 | 124 | | 32 | | May 8 | 130 | | 0 | |
| (38) | | | | | (38) | | | | |
| May 12 | | | | Heart denervated | June 4 | | | | Adrenals inactivated |
| May 27 | 150 | 42 | 52 | | June 5 | 120 | | 8 | |
| May 28 | 130 | | 46 | | June 7 | 144 | | 4 | Struggled several times |
| June 2 | 128 | 40 | | Cat not aggressive, crouching, ears back | June 9 | 138 | | 10 | |
| June 2 | | | 68 | | | | | | |
| June 4 | 130 | | 56 | Slight spontaneous struggle | | | | | |

| | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|
| (46) | | | | | (46) | | | | |
| June 11 | | | | Heart denervated | June 24 | | | | Adrenals inactivated |
| June 15 | 136 | | 74 | Moderately active only | June 25 | 112 | | 8 | Struggling 15 seconds |
| June 19 | 128 | | 40 | | June 28 | 100 | 10 | 8 | |
| June 21 | 124 | 42 | | Appeared unafraid of dog | June 30 | 96 | | 12 | |
| June 21 | | | 44 | | July 6 | 114 | | 8 | Vigorous reaction |
| June 24 | 126 | 26 | 40 | | | | | | |
| (49) | | | | | (49) | | | | |
| June 10 | | | | Heart denervated | June 24 | | | | Adrenals inactivated |
| June 15 | 120 | | 112 | Spontaneous struggle | June 25 | 114 | | 4 | |
| June 16 | 126 | | 72 | | June 28 | 101 | 3 | 7 | Usual reactions |
| June 21 | 100 | 42 | | Brisk reaction to dog | June 30 | 110 | | −2 | |
| June 21 | | | 98 | | | | | | |
| June 24 | 118 | 26 | 60 | | | | | | |

increases, and 5 if the decreases are counted as zero (see fig. 2 in which the average is marked at 5).

Related to the foregoing increments of heart rate are results noted when a stomach tube was passed for the purpose of introducing cold water (see Cannon, Querido, Britton and Bright, 1926). Usually this was accompanied by some resistance on the part of the animal. The pulse was raised to varying degrees; in one animal with a respiratory infection the increase was only 22 beats, in two others it varied from 32 to 56, and in a fourth the increases were 76, 116, 124 and 132 on four different occasions. After exclusion of medulliadrenal influence the maximal increase under the same conditions in the same animals was 10 beats per minute.

Struggle in the holder offers a favorable condition for determining the latent period of the response to excitement, for the position of the animal permits a record of the heart as soon as the struggle ceases, and, as stated above, the effort is usually brief. Acceleration of the denervated heart from reflex medulliadrenal secretion begins in about 8 seconds and reaches a maximum in about 35 seconds (Cannon and Uridil, 1921). As shown in figure 4, the rise of heart rate after struggle takes a similar course if the adrenal glands are intact, and fails if they are not functioning.

*Persistence of the excited state after disappearance of the exciting condition.* A striking feature of the influence of emotional disturbance on gastric secretion is the continued inhibition, lasting long after the apparent excitement has subsided. For example, Bickel and Sasaki (1905) noted that, whereas sham feeding of a dog for five minutes caused during the following twenty minutes a flow of 66.7 cc. of gastric juice, sham feeding for the same time, but after five minutes of exciting experience with a cat, caused during the next twenty minutes a flow of only 9 cc. of a juice rich in mucus; and when the excitement followed the sham feeding the inhibition was nearly complete. It was this persistence of the visceral disturbance after the occasion for it had passed that led to the first observations on the emotional secretion of adrenin, for it had seemed possible that the lasting effect might be due to circulating adrenin which would continue by chemical action the changes initiated by nerve impulses (see Cannon, 1915, p. 40). The common experience that calmness and serenity are not restored at once after a period of great emotional stress, that a state of uncontrollable agitation persists, was related to that suggestion. It was a matter of considerable interest, therefore, to learn whether adrenal secretion did in fact go on for some time after the obvious excitement had ceased—an enquiry made readily possible by study of the denervated heart.

The most favorable condition for learning fairly the influence of strong emotion on the course of medulliadrenal secretion was that of the caged cat attacked by the dog. The signs of emotional upset were maximal, the big muscles were not used so much as in the struggle on the holder, and

as soon as the brief fray was ended the cat could be placed on a cushion and the heart beat could be recorded at regular intervals without any further annoyance. As illustrated in figure 5, a high heart rate is found immediately after the removal of the excited cat from the cage. The increased rate rapidly falls, but not sharply to the basal level. That level may not be reached for twenty or twenty-five minutes after an exciting experience which itself lasts only a minute. After the adrenal glands were inactivated, even though the experience in the cage was

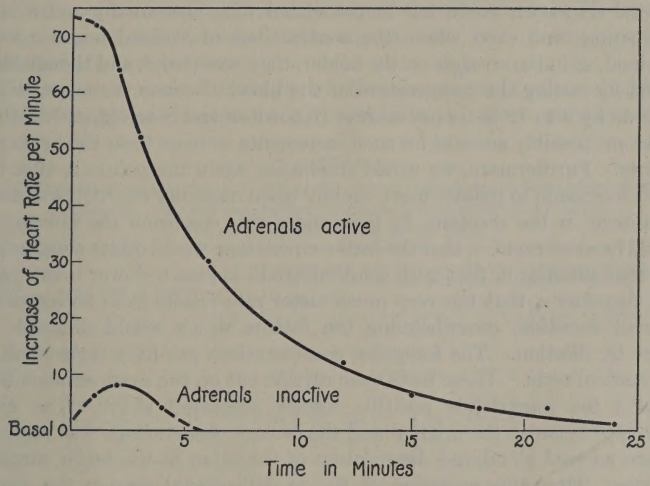


Fig. 5. Long persistence of the faster heart rate, when the adrenals were active, after the animal (cat) was excited by a barking dog for one minute. Only slight increase of heart rate and its relatively rapid subsidence, after adrenal inactivation, though the cat was excited twice as long as before. In both instances the animal was promptly removed from the cage after the excitement, and during the period of recovery rested quietly on a cushion.

extended to two minutes, the increment of heart rate, as shown in figure 5, was 8 beats as compared with 72 beats before the inactivation, and the basal was recovered within ten minutes as compared with twenty-five minutes previously.

Five animals which had struggled on the holder for less than ten seconds were thereafter studied while quiet on a cushion. After ten minutes the increase of heart rate was still 12 or more beats per minute in all these cases, and after twenty minutes it was still 2 to 6 beats above the basal in three of them.

The return to the former quiet state occurs sooner when the adrenal response is less intense. For example, in cat 26, an excitement which caused an increase of 40 beats was recovered from in ten minutes, whereas one which caused an increase of 62 beats had not completely subsided at the end of fourteen minutes (see table 4).

Discussion. That the faster beating of the denervated heart in the circumstances described above was due to increased adrenal secretion is proved by a variety of considerations. It could not have been due to increased temperature, for the minor movements and the almost pure visceral responses would not be associated with noteworthy quick heat production; and even where the contractions of skeletal muscles were maximal, as in the struggle on the holder, they were brief, and though they might by raising the temperature of the blood 1° cause the heart to accelerate by 6 to 12 beats per minute (Knowlton and Starling, 1912), they could not possibly account for such increments as more than 100 beats per minute. Furthermore, we would emphasize again the points *a*, that the heart was made to pulsate most rapidly when muscular exertion was most prominent in the reaction; *b*, that under this condition the circulation would be most rapid; *c*, that the faster circulation would dilute a uniformly secreted adrenin; *d*, that such dilution would induce a slower heart rate, and therefore *e*, that the very much faster rate results from an increased adrenal secretion, overwhelming the factors which would diminish its effect by dilution. The foregoing considerations are fully supported by our control tests. These tests were carried out on the same animals that yielded the remarkable positive results presented above. The only difference between the original and the control observations was removal of one adrenal gland and denervation of the other in the latter circumstances. After this exclusion of the medulliadrenal agency the faster pulse wholly failed to occur or was so slight as to be explicable by a rise of temperature. These results fully confirm the earlier evidence, brought forward in these laboratories and elsewhere, that as a part of the reaction of the organism in great excitement there is a striking increase of the discharge of adrenin from the adrenal medulla.

One of the most surprising of our results was the involvement of the adrenal medulla in merely slight muscular activities. Doubtless the reason why the heart rate was not basal when the cat was taken from the floor and set on the cushion was that the animal had just before been moving about, or had resisted being picked up; the average drop in heart rate was about the same as the increase caused by walking. This close association of adrenal secretion with movement brings up again the question of its service in the organism. Evidence obtained in these laboratories that adrenin is able to produce a rapid recovery of the capacity of fatigued muscle to respond to stimulation (see Gruber, 1914)—an effect interestingly

related to recent testimony as to the beneficial influence of sympathetic impulses on fatigued muscle (see Orbeli, 1923)—as well as considerations that fear and rage might be preparatory for flight or attack, had led to the inference that emotional stimulation of medulliadrenal secretion is favorable to prolonged muscular effort (Cannon, 1914). The increased secretion of adrenin accompanying incidental and routine muscular movements such as walking, its greater concentration in the blood during muscular exercise (see Hartman, Waite and Powell, 1922) and its abundant outpouring as a consequence of vigorous struggle emphasize the probable significance of adrenin for efficient use of muscles in the body. We are now endeavoring to discover what value adrenin may have in the course of continued physical exertion.

The results reported in table 3 prove that the output of adrenin is greatest when emotional excitement is combined with violent struggle. Un-

TABLE 4

*Cases illustrating the slow recovery of the basal rate of the denervated heart after emotional excitement. During observation the animals were quiet on a cushion. The adrenals were active in all cases*

| CAT NUMBER | DATE, 1926 | BASAL HEART RATE | INCREASE OF HEART RATE ABOVE BASAL AT STATED MINUTES AFTER CAT CAGED AND EXCITED BY DOG FOR 1 MINUTE | | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | | | 1 m.* | 2 m. | 4 m. | 6 m. | 8 m. | 10 m. | 12 m. | 14 m. | 16 m. | 18 m. | 20 m. | 22 m. |
| 26 | Mar. 10 | 128 | 40 | 32 | 18 | 8 | 2 | 0 | | | | | | |
| 26 | Mar. 18 | 98 | 62 | 42 | 30 | | 12 | 10 | 2 | 2 | | | | |
| 26 | Mar. 19 | 116 | 44 | 36 | 16 | | 6 | | 2 | 0 | | | | |
| 27 | Mar. 18 | 120 | 72 | 64 | 52 | 30 | | 18 | 12 | 6 | 4 | | 4 | 1 |
| 33 | Apr. 16 | 118 | 34 | | 18 | 10 | 4 | | | | | | | |
| 46 | June 24 | 126 | 26 | | | | 18 | | 4 | | | | | |

* Approximately correct.

fortunately we have not been able to contrive an experiment in which medulliadrenal secretion can be estimated after great muscular effort without attendant excitement. The secretion incidental to vigorous activity and that resulting from the intense emotional state, therefore, cannot now be separated. As shown in table 2, however, the output is considerably less when the visceral manifestations of emotional stress are not accompanied by effort. These results coincide with those reported for pseudaffective medulliadrenal secretion; when the preparation was "quiet," though paws were wet with sweat and hairs were erect, the average rate of the denervated heart was 222, and when the preparation became active the rate rose to 252 (Cannon and Britton, 1925). Since increased secretion of adrenin is evidence for increased discharge of sympathetic impulses to the adrenal medulla, and since the sympathetic system is organized for

general and diffuse discharge (see Cannon, 1915, p. 26) even if the circulating adrenin did not have that effect, it follows that the bodily processes are much more profoundly altered in the full expression of emotion, i.e., in adaptive visceral changes *plus* vigorous effort, than in the preparatory visceral changes alone. This fact gives support to the suggestion made by Cannon and Britton (1925) that when limitation of the bodily disturbances is desirable, control of the controllable factors, the voluntary muscles, would minimize the effects of an emotional storm. It is clear that this new evidence modifies earlier advice, based on the theoretical desirability of completing a physiological process, that the bodily changes due to excitement should be "worked off" by strenuous exertion.

The results reported above offer another interesting hint. It is sound doctrine that the organism profits by the exercise of the functions of its parts. The deep stirring and unsettling of the routine of quiet existence, wrought by great excitement, may be as important for proper service of the viscera as is work for the proper service of muscles. One might argue, therefore, that occasional intense excitement is a physiological need. Strong physical effort, however, operating either directly *via* a larger sympathetic discharge or indirectly *via* increased output of adrenin, can influence the viscera perhaps nearly as well as excitement alone. Thus exertion is favorable to bodily welfare not only by bringing into use the muscular mechanisms, but also by requiring those internal adjustments, commonly the consequences of emotional excitement, which contribute to muscular efficiency.

The persistence of the visceral concomitants of excitement for some time after the stimulus for them has ceased to act, was attributed solely to a continued adrenal secretion. Evidence not yet ready for publication indicates that under normal conditions, with the cervical sympathetic connections intact, the thyroid gland also may play a rôle in causing the emotional upset to continue long after the initiating experience. This extension of the visceral disturbances in time has bearings on conduct in an exciting situation, as well as thereafter. It points out the natural effect of the full expression of fear or rage, and shows the importance of limiting that expression if a persistent state of disquiet is to be avoided. It also corroborates the counsel that when bodily functions are dominated by sympathetic influences, as in the more powerful emotions, the exercise of opposed function should not be attempted. Thus the digestive processes, which are inhibited by excitement, may continue to be disturbed for a considerable period, and digestion can not proceed properly until a state of calm has been restored.

The studies on medulliadrenal secretion described in previous papers from these laboratories have been identified with the "emergency theory" of the sympathico-adrenal functions—i.e., with the view that these func-

tions are made to operate in times of stress, when they facilitate and reinforce the laboring muscles (Cannon, 1914). The involving of these functions in slight muscular contractions might be regarded as invalidating the theory. The essentials of the theory, however, were that the changes wrought in the organism at critical moments—the shifts in the circulating blood, the hyperglycemia, the dilated bronchioles, the more rapid heart beat, the flush of adrenin—were favorable to highest efficiency in supreme muscular exertion. That all these changes may occur to some small degree, even when an animal rises from repose and moves about in a simple and ordinary manner, indicates that what takes place on a large scale in emergencies takes place on a small scale in the common behavior of the organism. We can hardly conceive that slight efforts are given a critical importance because the heart has been denervated—they appear to be too slight to justify that interpretation. That being assumed, therefore, the emergency theory would have to be altered insofar as it might imply that the sympathico-adrenal mechanism is called into action *only* at times of violent emotion. According to the evidence now in hand, the greater the emergency, as measured by intensity of excitement and struggle, the more is that mechanism utilized.

## SUMMARY

The evidence for and against emotional stimulation of medulliadrenal secretion is reviewed and the desirability of securing further evidence is made clear.

The advantages of the lasting preparation of the denervated heart are pointed out: *a*, the acceleration is slight (about 10 beats per minute or fewer) if thyroid, hepatic and medulliadrenal factors are excluded; *b*, the faster heart beat which occurs when medulliadrenal secretion alone is admitted to action and is stimulated justifies the use of the heart as an indicator of an increase of that secretion; *c*, the denervated heart permits a graphic record to be made which displays the latent period, the peak of activity, and the gradual subsidence of the humoral response; *d*, the observations may be repeated again and again on the same animal under normal conditions; *e*, control tests can be made on the same animal after inactivation of the adrenals (by removal of one and denervation of the other); and *f*, the increased heart rate can reasonably be interpreted as a rough measure of the increase of adrenin in the blood, for the faster circulation which would accompany increased secretion of adrenin would be unfavorable rather than favorable to its causing the cardiac acceleration.

Minor movements of the cat with denervated heart, such as extending the legs or turning the body, were accompanied by increases of heart rate of 5 to 10 beats per minute; walking made the rate faster by 10 to 20 beats. The average increase in 27 tests was 15. No signs of emotional disturb-

ances were noted. After adrenal inactivation the same activities were accompanied by very slight acceleration or none at all—the average in 23 tests was 1 beat per minute (see table 1 and figs. 1 and 2).

Emotional excitement, such as may be aroused by bringing near the cat a barking dog, or by restraining the animal in a holder, and manifested by erection of hairs and minor movements (e.g., hissing, snarling, retraction of the ears, baring of the teeth, or restless twitching of the tail) was accompanied by a faster heart rate. The increment varied roughly between 15 and 30 beats in the presence of the barking dog and between 10 and 35 beats during restraint in the holder. The average rise in 45 tests was 22. The variations of rate corresponded with variations in other signs of emotional reaction. After inactivation of the adrenal glands repetition of the same conditions with the same animals induced only minor accelerations, or none at all, or, in some instances, a small decrease of heart rate (see table 2 and figs. 1 and 2). The average in 39 tests was 2.

Great emotional excitement *plus* vigorous activity, brought about by letting a dog bark at the cat when caged, or by causing the cat to struggle in the holder, though it lasted only a minute or less, caused the heart rate to increase, in the former condition between approximately 30 and 50 beats per minute, and in the latter between approximately 40 and 80. The average rise in 53 tests was 49. After the medulliadrenal factor had been excluded, the rise of rate was usually 8 beats or fewer, and in some tests the heart worked more slowly after the struggle than before (see table 3 and figs. 1, 2, 3 and 4). The average rise in 43 tests was 5.

After a cat has been caged and excited by a barking dog outside, the disturbance thus induced may persist for twenty or twenty-five minutes, although the animal meanwhile is resting quietly on a cushion (see table 4 and fig. 5).

In the discussion some practical inferences are drawn from the foregoing observations.

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